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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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10/520,809

02/02/2005

Koji Kawai

TOR-04-1339

9964

35811 7590 09/17/2008  
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EXAMINER

GEMBEH, SHIRLEY V

ART UNIT

PAPER NUMBER

1618

MAIL DATE

DELIVERY MODE

09/17/2008

PAPER

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

<b>Office Action Summary</b>	<b>Application No.</b> 10/520,809	<b>Applicant(s)</b> KAWAI ET AL.	
	<b>Examiner</b> SHIRLEY V. GEMBEH	<b>Art Unit</b> 1618	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☒ Responsive to communication(s) filed on 22 August 2008.
- 2a) ☐ This action is **FINAL**.                      2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) 11, 12, 14 and 16 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 11-12, 14 and 16 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All    b) ☐ Some \*    c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

### Attachment(s)

- |  |   |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)          | 4) <input type="checkbox"/> Interview Summary (PTO-413)           |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____                                      |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)          | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date _____  | 6) <input type="checkbox"/> Other: _____                          |

## **DETAILED ACTION**

### **Withdrawal of Finality**

The response filed on 8/22/08 presents remarks and arguments. Applicants' request for reconsideration of the rejected claims in the last office action dated 5/29/08 has been considered.

The response filed on **8/22/08** presents remarks and arguments to the office action mailed on **5/29/08**. Applicant's request for reconsideration of the rejection of claims in the last office action has been considered.

Applicant's arguments have been fully considered but they are not deemed to be persuasive. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The following rejections and/or objections are either reiterated or newly applied. They constitute the complete set presently being applied to the instant application.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

### **Status of claims**

Claims 1-10 are cancelled.

Claims 11-12, 14 and 16 are pending. Claims 11 and 16 are amended.

.

***Withdrawn Claim Rejections - 35 USC § 103***

Art Unit: 1618

Claims 11-12, 14 and 16 rejected under 35 U.S.C. 103(a) as being unpatentable over Portuguese et al. US 5, 352,680 (of record) taken with of Rudd et al. Europ. J. Pharm. (of record) in view of Neeleman, European Society of Anesthesiologists (newly applied) as evident by Meijer et al., Brain Research, Vol. 868(1) 2000 135-140 Abstract only. The rejection is withdrawn.

Applicant's main argument is that nicotine is used to cause emesis and not fentanyl. Applicant also shows the conflicting result in the Rudd et al Reference. Page 7 of the remarks states: Applicant discovered that naltrindole can selectively treat nausea and vomiting caused by mu-opioid receptor agonist morphine without suppressing the analgesic effect of morphine. This is merely a statement and not a fact as no evidence or data illustrating the showing is given, thus no consideration is given to such a statement without factual evidence. Upon further search a new rejection is made below.

### ***Claim Rejections - 35 USC § 102***

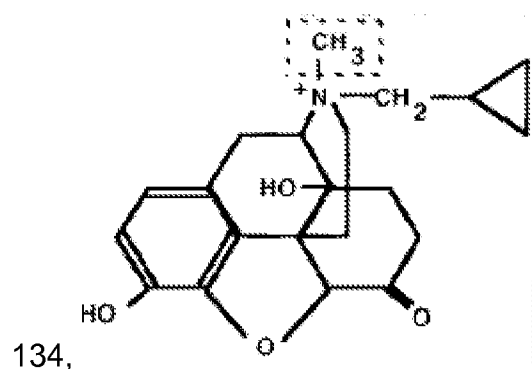
The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 11, 14 and 16 are rejected under 35 U.S.C. 102(b) as being anticipated by Yuan et al. Drug Development Research 50:133-141, 2000.

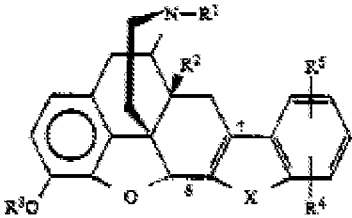
The reference teaches with regard to instant claims 11, 14 and 16 morphine a mu-opioid agonist induces vomiting. See underlining abstract and introduction. The reference further discloses that the morphian derivative methyl-naltrexone completely inhibited the emetic effect of morphine. See page 135 underlining. Please note that morphine is described as a mu-receptor agonist in claim 16. Please see Fig. 1, page



Claims 11-12, 14 and 16 are rejected under 35 U.S.C. 102(b) as being anticipated by Portoghese et al. US 5, 352,680 (of record).

Portoghese et al. teach a compound that is structurally identical to that of the

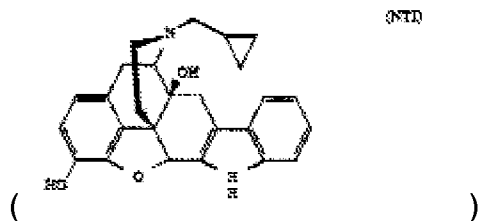
claimed compound as



(see col. 14, lines 10 +) as in claims 11 and 12, where R<sup>1</sup> is an alkyl group having 1-5 carbon atoms, R<sup>2-4</sup> are hydrogen, or R<sup>4</sup> and R<sup>5</sup> together form an O, (as in claim 14) R<sup>6</sup> is hydrogen and Q is



(see col. 14 lines 10-30). One specific compound is naltrindole



The reference teaches the adverse effect of morphine (as required by instant claim 16, see col. 1, lines 15-24, wherein one such effect is vomiting, thus treating nausea and vomiting (see col. 1, lines 34-43) and the  $\mu$ -opioid agonist compound, is morphine (see col. 9 lines 8-17). Portoghese et al. teach the above compound is an opioid antagonist and belongs to a group of morphinan derivatives.

### ***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.

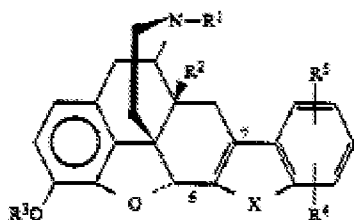
Art Unit: 1618

4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 11-12, 14 and 16 are rejected under 35 U.S.C. 103(a) as being unpatentable over Yuan et al. Drug Development Research 50:133-141, 2000 in view of Portoghese et al. US 5, 352,680 (of record).

Yuan et al is applied here as above. The Yuan reference fails to teach the compound embraced by instant claim 12, therefore Portoghese as it teaches the compounds embraced by the instant claims 11-12 and 14.

Portoghese et al. teach a compound that is structurally identical to that of the



claimed compound as

(see col. 14, lines 10 +) as in

claims 11 and 12, where R<sup>1</sup> is an alkyl group having 1-5 carbon atoms, R<sup>2-4</sup> are hydrogen, or R<sup>4</sup> and R<sup>5</sup> together form an O, (as in claim 14) R<sup>6</sup> is hydrogen and Q is



(see col. 14 lines 10-30).

The reference teaches the adverse effect of morphine (as required by instant claim 16, see col. 1, lines 15-24, wherein one such effect is vomiting. If a ligand acts at a single opioid receptor type or subtype, the potential side effects mediated through other opioid receptor types can potentially be minimized or eliminated. Thus

Art Unit: 1618

treating nausea and vomiting (see col. 1, lines 34-43) and the  $\mu$ -opioid agonist, compound is morphine (see col. 9 lines 8-17). Portoghese et al. teach the compound is an opioid antagonist and belongs to a group of morphinan derivatives.

One of ordinary skill in the art would have been motivated to combine the teachings of Yuan et al with that of Portoghese and administer the drugs of Yuan and Portoghese to patients suffering from nausea and vomiting induced by or caused by a mu-opioid receptor agonist. As taught in the art these agents are employed to counter the nausea effect induced by morphine.

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to SHIRLEY V. GEMBEH whose telephone number is (571)272-8504. The examiner can normally be reached on 8:30 -5:00, Monday- Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, MICHAEL HARTLEY can be reached on 571-272-0616. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.



Art Unit: 1618

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Michael G. Hartley/  
Supervisory Patent Examiner, Art Unit 1618

/S. V. G./  
Examiner, Art Unit 1618  
9/11/08